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(54) Title: SOLAR AND FULL SPECTRUM BLOOD IRRADIATION DEVICE AND METHOD

(57) Abstract

A method and device for irradiating a sample, such as blood, with solar and/or full spectrum radiation. The device allows for the even and thorough irradiation of a sample such as blood, in an extra-corporeal manner without the use of costly anticoagulants. The invention may be used in the treatment of infectious, inflammatory, and circulatory disorders.

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SOLAR AND FULL SPECTRUM BLOOD IRRADIATION DEVICE AND METHOD

TECHNICAL FIELD AND INDUSTRIAL APPLICABILITY OF THE INVENTION

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This invention relates generally to a method of irradiating the blood with solar and/or full spectrum radiation, and specifically to a device that uses solar and/or full spectrum radiation to stimulate the irradiated blood cells for the treatment of infectious, inflammatory, circulatory, and other disorders. The present device 10 provides a low cost method that avoids the drawbacks of previous blood irradiation therapies.

BACKGROUND OF THE INVENTION

15 Blood irradiation (BI) therapy has a long history. It was first employed in the early 1920s by scientist Emmet K. Knott and his medical colleagues; Knott used an ultraviolet BI (UBI) device (U.S. Pat. No. 1,683,877) to irradiate, in an extracorporeal mode, a small amount of blood that was then returned to the body through a vein. This design found its fullest embodiment in the Knott Hemo-Irradiator (U.S. Pat. No. 20 2,309,124).

25 The activated blood cells resulting from such therapy were found to achieve a beneficial effect by various mechanisms including oxygenation of the blood, destruction of microorganisms, normalization of the components of the blood via the effects of the secondary radiation emitted from the irradiated blood cells, suppression of inflammation, improvement of microcirculation, and stimulation of hematopoiesis. Accordingly, UBI was used by many American practitioners until the 1950s when it was set aside presumably in favor of antibiotics and vaccines. In recent years, 30 interest in such therapy has revived, as exemplified by the device disclosed in United States Patent No. 5,459,322, which provides an apparatus for exposing a blood sample to ultraviolet radiation.

Similar devices came to be used in Central Europe. In the 1970s Russian investigators began to study the uses of UBI, and in the 1980s the Russian-made Izolda UBI device gained wide acceptance among Soviet physicians. Subsequently, Russian and Ukrainian physicians began to use intravascular low-intensity lasers to 5 irradiate blood (LBI), with roughly the same effects. The low-intensity laser offers the advantage of being a hand-held device that is easy to use and does not require an irradiation chamber or the trouble and expense of using anticoagulants. Additionally, with LBI, the amount of irradiation may be calculated precisely. Despite these positive advances, the device has the drawback and concern of creating damage to 10 red blood cells even when used at a very low intensity.

Administration of LBI has involved a number of approaches. The most effective one entails 30-minute sessions of a helium-neon laser of 632.8 nm with 1-5 milliwatt output at the tip of a polymer-coated quartz waveguide (ranging from 200 to 15 600 micrometers in diameter) inserted into a vein with an IV needle. Further, for certain localized conditions, LBI appears to be more effective than local low-intensity laser therapy. A study of the effects of the two approaches in treating degenerative diseases of the lower extremities concluded that LBI was distinctly superior to local laser therapy (G.E. Brill, Saratov [Russian] The Experimental and Clinical Use of Low- 20 Intensity Lasers and Irradiation in the Millimeter Range, (1994), p. 148). According to another study in the same reference, LBI via transdermal irradiation of a vein with an infrared laser of a longer wavelength (830 nm vs. the normal 632.8 nm) provided measurable results while avoiding the invasiveness of an IV needle and waveguide 25 as the longer wavelength permitted deeper penetration in order to irradiate the blood more effectively. But the results were not nearly as good as with intravenous LBI (*Ibid.*, pp. 140-3).

One concern in regard to intravenous LBI is that the fiber waveguide, which commonly extends 2-5 cm downstream in the vein from the point of insertion, could 30 become a source of transmission of infection to other patients, especially in countries with a relatively high incidence of HIV, in spite of vigorous cleaning.

Another blood irradiation method known as photopheresis or extracorporeal photochemotherapy uses photoactive drugs, filters, and separation of white blood cells from red blood cells. In effect, photopheresis is a combination of UBI and chemotherapy in which the secondary radiation triggers the photoactive drug previously taken up by the target cells. Thus, to achieve the same effect, photopheresis uses less irradiation and more chemotherapy than UBI. The substances used are generally psoralens, which occur in nature but are used in chemotherapeutic concentrations that can have more toxic effects than other forms of BI (Edelson, R., New England Journal of Medicine, 316: 297-303, "Treatment of Cutaneous T-Cell Lymphoma by Extracorporeal Photochemotherapy" (1991)). Photopheresis has the advantage that it is approved by the FDA for the treatment of cutaneous T-cell lymphoma and is currently in clinical trials for other indications. Examples may be found in United States Patent No. 5,426,116 and 5,593,823. Its use ranges from inactivation of pathogens in blood using photoactivation and psoralens as found in U.S. Patent No. 5,593,823 to a method of treating atherosclerosis as in US. Patent No. 5,426,116. The basic technique uses low-intensity fluorescent sources of UV-A and is employed in many major medical centers.

Over the last 70 years millions of patients have been treated in Russia, Ukraine, Germany, and the United States with no systematic toxicity of BI having been identified. While BI often appears to gain in efficacy from a placebo-like effect, many clinical studies have shown that it has a consistent, powerful pharmacological effect as well.

The assessment of the effects of irradiation on living cells has long followed the theory of action spectra, but there is evidence suggesting that the effects are more subtle. The general theory of photobiology that developed in the early decades of the 20th century was based on a somewhat mechanistic view of living cells. One result was that scientists have sought to identify absorption and action spectra for various tissues, which in turn led the developers of ultraviolet and laser BI devices to focus on certain wavelengths that were presumed to convey a superior effect. This mechanistic approach failed to take into account aspects of the interaction of

irradiation and living cells that were not included in the concept of absorption or action spectra, or in the "laws" of photochemistry.

Two recent studies are of interest in this regard. A series of clinical trials
5 carried out in Russia comparing the efficacy of UBI and LBI together with fasting in
the treatment of bronchial asthma and chronic bronchitis repeatedly found the same
result: that LBI has more rapid action than UBI but that UBI is ultimately more
effective (G.I. Sukhanova, ed. *Laser Therapy in the Far East* [Russian]. Vladivostok:
Dal'nauka, 1993--see especially pp. 67-68).

10

In addition, there is evidence that solar irradiation affects living cells in ways
that cannot be explained by action spectra alone, and that solar irradiation has
therapeutic properties superior to those of artificial sources. A Finnish study found
that heliotherapy was decisively superior to artificial UV therapy in the treatment of
15 psoriasis, for instance (E. Snellman, "Comparison of the Antipsoriatic Efficacy of
Heliotherapy and Ultraviolet B: A Cross-over Study," *Photodermatology,
Photoimmunology, Photomedicine* 1992, No. 9, pp. 83-85). The researcher
suggested that certain UV-A wavelengths might explain this deviation from the
equivalence between solar and artificial UV irradiation that established action spectra
20 ordain, but it is equally possible that such aspects of solar irradiation as coherence
length, polarization, and magnetic field are involved.

Thus, there are grounds for believing that full spectrum and solar irradiation
can more fully activate blood cells than ultraviolet and laser irradiation alone, thereby
25 conveying a superior therapeutic effect.

Historical and current UBI devices have various drawbacks, derived largely
from their throughput method of running the blood past a UV source. Running the
blood through a cuvette for irradiation in a device creates the difficulty of cleaning the
30 cuvette and the danger of transmission of infectious agents. The use of disposable
cuvettes is expensive, so it will tempt practitioners without sufficient resources to
reuse them, thereby transmitting infections.

In addition, the devices are generally operated within sight of the patient, which can increase patient discomfort leading to problems such as nausea and fainting. They also are operated entirely by medical personnel, with the patient left as a passive bystander. Lastly, the tendency of the blood to coagulate can cause 5 disruption of therapy in the UBI devices. This necessitates the regular use of expensive anti-coagulants such as heparin. Anticoagulants are not only difficult to obtain in many countries, but they also add to the complexity of the procedure by complicating the administration of UBI therapy.

10 The many efforts made by inventors of UBI devices to ensure that the blood cells receive even, thorough irradiation also add to the expense of the devices and often leave certain cells under-irradiated. Moreover, attempts to provide a precise dose have been less than successful because of variations in the speed and sequence with which blood is conveyed through the devices and because of 15 variations in the amount of blood irradiated.

Accordingly, a need exists for a new approach that reduces or eliminates the need for anticoagulants while improving the thoroughness of the irradiation. These requirements are fulfilled by the method and device of the invention described below.

20 The present invention also provides a device that is totally portable such that it may be used in the field while ensuring even, thorough irradiation.

SUMMARY OF THE INVENTION

25 The present invention comprises an apparatus and method for the solar and full spectrum irradiation of blood cells. A full spectrum light source is pivotally mounted on a support above a rotatable transfusion bag holder that can be rotated by means of knobs as on a typewriter. Underneath the cage is a metal reflector that is 30 attached on both sides of the device to the pivot point so that it can be turned in an arc and held in place by friction. The cage is opened to insert a transfusion bag with blood, then closed with a latch. The full spectrum light then irradiates the blood as the knob is turned in order to expose all the cells evenly and avoid coagulation.

When the therapeutic dose of full spectrum light is administered, the transfusion bag is removed in order to return the blood to the body.

For operation in solar mode, a measurement of solar irradiation intensity is 5 made with an incident light meter in order to calculate the correct exposure time for a therapeutic dose. The full spectrum light is rotated out of the way, the transfusion bag is inserted, the reflector is rotated to face the sun, and a knob is turned until the therapeutic dose is received.

10 BRIEF DESCRIPTION OF THE DRAWINGS

Referring now to the **FIGURE**, the full spectrum light 1 consists of an ultraviolet fluorescent tube 2 and a visible and infrared fluorescent tube 3, as well as a shade 4 with an inside reflective surface. The full spectrum light 1 can be folded 15 out of the way during the solar mode by turning it on its pivot 5. The metal base 6 has two triangular sides 7 and 8 between which is inserted a cage 9 turned by a knob 10. The cage 9 has a latch 11 that permits it to be opened to insert the transfusion bag 12. The central portion of the cage has indentations 13 and 14 on both sides to squeeze the transfusion bag 12 and prevent it from sliding during cranking.

20 A metal reflector 15 with polished inner surface 16 is attached to the sides 7 and 8 at pivot 5 so as to rotate in order to aim it to reflect solar irradiation in the solar mode. A sliding drawer (**not shown**) in the base 6 contains storage space for an incident light meter and other items. The base 6 also contains the ballast (**not shown**) for the full spectrum light 1. A switch 17 operates the light.

DETAILED DESCRIPTION AND PREFERRED EMBODIMENT OF THE INVENTION

30 A preferred embodiment of the apparatus and method in the treatment of a patient of 70 kg with an infectious disease, for example, is to decide first whether to use the solar mode or the full spectrum mode, in keeping with the medical condition, availability of sunlight, and patient's wishes. The full spectrum mode of the current invention is high in precision, especially since it will ordinarily be administered indoors

where the temperature, which can affect the output of the fluorescent lights, can be controlled. Various UBI devices and the solar mode of the current invention are less precise, but the potential for superior efficacy and lower toxicity of the solar mode of the current invention offsets its lower precision. Those knowledgeable in the art are 5 aware that BI therapy relies more on the practitioner's judgment and evaluation of the patient's condition than do chemotherapies dosed according to standard protocol. BI's therapeutic effect can much more closely correspond to the frequency and intervals at which the treatment is repeated than to the precise dose.

10 **Example I – Use of the Device in Solar Mode**

If the solar mode is indicated, then the device should be set up on a table outdoors. The intensity of solar irradiation is measured with an incident light meter, and the full spectrum mode's standard therapeutic dose is divided by this intensity to 15 yield the number of minutes for a therapeutic dose at that intensity of solar irradiation. The therapeutic dose is determined by iterative testing of various levels beginning with very low ones. A typical low level to begin with would be 1 minute exposure. An endpoint indicator of when a too high level is being reached is as described in the Knott technique. Specifically, when the blood is reinfused into the patient and the 20 patient flushes, then the high endpoint has been reached and should not be exceeded. (The assumption is made that time and intensity of irradiation trade off against each other as each varies so as to yield roughly the same therapeutic result.) If the patient so desires and is in a suitable condition, he/she may be taken outside in a bed or chair. Otherwise, the blood may be withdrawn inside and carried quickly and 25 under steady movement by the nurse outside to the device; or a window can be opened in such a way as to permit direct solar irradiation of the blood (glass will block UV rays and thereby diminish the therapeutic effect).

175 ml of blood (2.5 ml per kg) is withdrawn from the antecubital vein into a 30 200-ml capacity transparent, polypropylene transfusion bag. The bag and needle hull are capped with sterile caps; according to the judgment of the nurse, saline solution may first be injected into needle, bag, or both in order to lessen the chance of coagulation. Then the bag is placed into the cage 9, the latch 11 is closed, the full

spectrum light 1 is rotated out of the way, the device is aimed at the sun, and the reflector 15 is rotated in order to obtain maximum reflection into the blood. It should be noted that the reflector reduces the amount of time required to achieve a full dose, with the added benefit of reducing the time in which coagulation of the blood is an issue. The patient or the nurse slowly turns the knob 10 to rotate the cage 9 in order to ensure a gentle turbulence of the blood cells. This will provide an even and thorough irradiation of all cells, avoid damaging overexposure of any individual cells, and minimize the danger of coagulation. When the time of exposure has reached the therapeutic dose, the transfusion bag is removed from the device and the blood is reinfused through the vein.

The method and apparatus of the present invention make possible batch processing of blood contained in transfusion bags, which in turn conveys major benefits unavailable in past devices.

The transfusion bag should be transparent, preferably of polypropylene or some other material that permits passage of UV rays. The bag should be as thin as possible to permit the least blockage or distortion of solar and full spectrum irradiation. Ideally, the inside of the bag should be rounded like a pouch to deny the blood any corner or edge in which to coagulate. The bag should be optimally 200 ml in volume, though any size between 100 ml and 400 ml is also acceptable. Larger amounts can exceed the known limit at which BI therapy is very low in toxicity and should be used only in emergencies such as fulminating conditions. In these cases, several transfusion bags in a row can be used. Smaller bags--10-50 ml--may be employed in the treatment of infants and children.

The use of a transfusion bag will permit better transmission of irradiation than through devices using glass or quartz barriers because the plastic can be made very thin and because there will be no film buildup from use to use, which would necessitate cleaning or degrade the passage of irradiation. The use of a disposable transfusion bag also prevents transmission of infection and obviates the need for bulky disposable cuvettes. The relatively low cost of the transfusion bag makes the

present invention more affordable in countries with limited resources and lessens the likelihood that the transfusion bags will be reused, thereby transmitting infections.

5 The needle should have a large bore--16 gauge is appropriate--in order to lessen the chances of coagulation. The tubing should also have a large bore for the same reason.

10 As soon as the blood is returned to the vein, the transfusion bag, tubing, and needle are disposed of. If, despite precautions, coagulation should occur, the transfusion bag is immediately disposed of and a new one is used for newly drawn blood. The small doses (<200 ml) mean that the loss of blood in any such incident is minimal.

15 Any commercially available standard incident light meter can be used to measure solar irradiation. The light meter may also be integrated into the device.

20 The different intensities of solar irradiation at different latitudes, times of day and year, and levels of cloud coverage will mean that the duration of the treatment in solar mode can vary considerably. Unless there is changing cloud cover, the intensity of solar irradiation can be assumed to be fixed for the relatively brief time that the blood is exposed. Blood cells are highly reactive to irradiation of any kind, and can be presumed to be even more reactive to solar irradiation than to other kinds. Thus the duration of therapy will be much shorter than would permit significant changes in the intensity of solar irradiation or the location of the sun.

25 The solar mode of the present invention can operate under light cloud cover. Photons absorbed through clouds, from skylight, from ambient light, and from reflection will all activate blood cells, though it is thought that direct solar irradiation from a clear sky will have the best effect. In the solar mode, the device will save 30 money because the energy will be free and because there will be no need to replace fluorescent tubes. If so desired, the present invention can be employed solely in the solar mode, with consequent savings in energy and fluorescent tubes. This approach would reduce environmental waste and be suitable for patients who desire only

natural therapy, not available with current devices. It would then also be possible to use the device in remote settings outside of the range of electricity.

Example II – Use of the Device in Full Spectrum Mode

5

In the full spectrum mode, the reflector 15 is rotated to the bottom of its arc and the full spectrum light 1 is moved to the top of its arc. In order to lessen fluctuation of the UV portion of the full spectrum light 1, it is best to turn it on 5 minutes before irradiating the blood. The reflector should be a concave 30-45 degree 10 section of a circle, not a parabola because that might focus the reflected rays so much that they would damage the blood cells.

The shortest full spectrum lights currently available are 15 inches in length. If the device is smaller, it is best to provide two or three complementary fluorescent 15 tubes side by side. One arrangement for a smaller device with current lighting technology would be to have two tubes—one for UV and blue, the other for the remaining colors and infrared. Another arrangement would be three tubes—one for UV, one for visible light with a blue high point, and one for red and infrared. This approach has the added benefit of avoiding the early burnout of the UV portion of 20 current full spectrum lights that makes it necessary to discard them after perhaps 1,000 hours of usage if one desires a UV component, thereby wasting the capacity of their visible and infrared portions to burn for 15,000 hours. In the optimal configuration, the UV tube can be exchanged as frequently as necessary, perhaps every 1,000 hours, while the other tubes can serve their entire lives.

25

Highly sophisticated laboratory instruments can be used to measure the UV irradiation after 700-800 hours to ensure that the fluorescent tube is still operating at full capacity. In the field, however, simply placing the incident light meter on the reflector 15 can permit the operator to monitor it adequately to detect a decline in 30 output. The presence of two or three light sockets permits the device to be equipped as a UBI device, with one or more UV tubes; or to serve for some time with diminished but still adequate output even in the event that a single tube burns out. In this event, however, it will be necessary to increase the duration of the irradiation.

The therapeutic dose in the full spectrum mode can be calibrated either with reference to the very precise therapeutic doses of low-intensity lasers used for LBI or by an iterative testing of various levels beginning with very low ones. The standard 5 therapeutic dose (length of irradiation) is administered to 2 to 3 ml of blood per kilogram, which is at the low end of the traditional American "Knott technique" and at the high end of the amount commonly irradiated in Russia. For a simple case of mild viral pneumonia, 1 to 2 treatments should suffice. For a serious case of chronic hepatitis, 6 to 8 treatments might be required over the course of two months.

10

It is to be understood that the device and method according to the present invention can be employed for a very wide range of indications including the suppression of graft versus host disease, treatment of burns and nonhealing wounds, and in veterinary medicine. In addition, the device may be used for the irradiation of 15 fractions of blood and of other fluids, including samples obtained from donors.

In regard to how many treatments may be safely given, various Russian and German authors mention 15-20 treatments or even as many as 30. In the older European muscular injection method, up to 60 small doses (as little as 10 ml) were 20 given. With the present device, as long as there is an interval that will permit recuperation or replacement of sensitive cells – perhaps two months between treatments – BI can be used indefinitely in the case of a chronic disease that needs to be suppressed at regular intervals.

25

The use of UV-A and visible/infrared bulbs to comprise the full spectrum light minimizes any potential for injury to the operator that might arise in the use of powerful UV-B and UV-C bulbs. Still, the light shade 4 can be made deeper to ensure that no radiant energy – no matter how mild – strikes the operator.

30

Although no long-term studies of BI's effects have been done, BI is much lower in intensity and far less concentrated on a specific target than present day x-ray treatments. In addition, the relatively rapid turnover of the blood cell population also reduces the impact of BI. In contrast to x-rays, the UV radiation from the Russian

UBI device is much less ionizing; in UV-A devices, none of it is. None of the currently used LBI devices emits ionizing radiation.

In fact, logic and anecdotal evidence suggest that BI has a prophylactic action
5 against cancer similar to that of aspirin against colon cancer. There is also not a shred of evidence that properly dosed BI consistently damages any specific organ or tissue of the body such as lymph nodes other than the minor damage that it does to the membranes of many red and white blood cells. Even there, in applications such as the treatment of preeclampsia, there is evidence that it stabilizes membranes
10 against lipid peroxidation (Bednarskii, et al, Akusherstvo I Ginekologija, 6:18-22 [Russian], "The Use of Intravascular LBI in the Combination Therapy of Preeclampsia" (1995)).

The invention is not to be construed as limited to the particular embodiment
15 disclosed. Variations and changes may be made without departing from the spirit and scope of the present invention and are understood to be embraced by it.

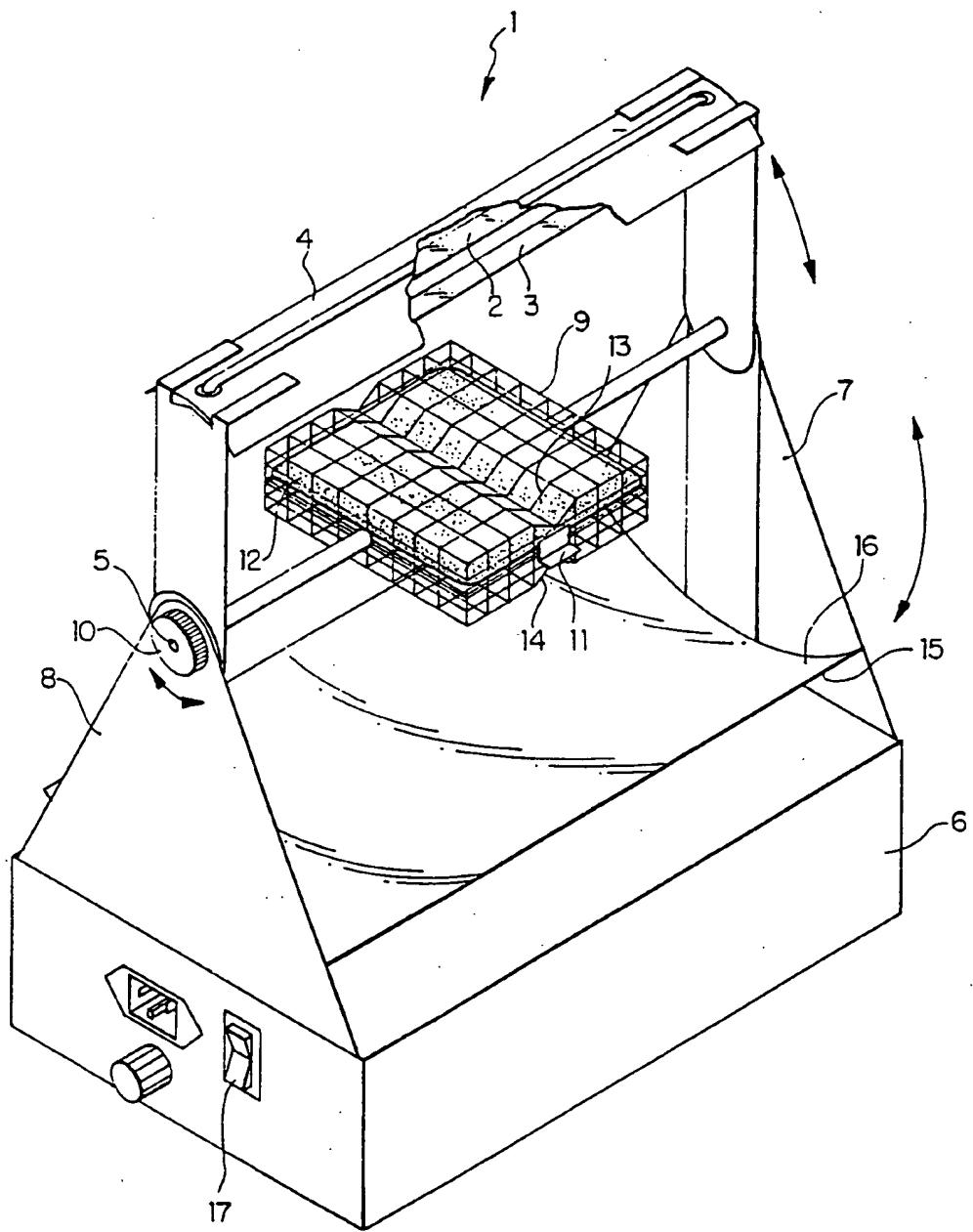
WHAT IS CLAIMED IS:

1. A method of irradiating a biological fluid sample with solar radiation comprising the steps of:
 - a) attaching a container containing said fluid sample to a rotatable sample holder
 - b) positioning said sample holder such that said container receives solar radiation from the sun
 - c) rotating said sample holder to agitate said fluid sample and achieve substantially uniform irradiation of said sample.
2. A method of irradiating a biological fluid sample with full spectrum radiation comprising the steps of:
 - a) attaching a container containing said fluid sample to a rotatable sample holder
 - b) positioning said sample holder such that said container receives solar radiation from the sun
 - c) rotating said sample holder to agitate said fluid sample and achieve substantially uniform irradiation of said sample.
3. A method as in claim 1, wherein said biological fluid is selected from the group consisting of blood, plasma, serum, platelet-rich-plasma or some other fraction of blood.
4. A method as in claim 2, wherein said biological fluid is selected from the group consisting of blood, plasma, serum, platelet-rich-plasma or some other fraction of blood.
5. The method of claim 1, wherein said container for containing the biological fluid sample is a blood transfusion bag.
6. The method of claim 2, wherein said container for containing the biological fluid sample is a blood transfusion bag.

7. A method as in claim 1 for treating infectious, inflammatory, and circulatory disorders.
8. A method as in claim 2 for treating infectious, inflammatory, and circulatory disorders.
9. An apparatus for irradiating samples of biological fluids with solar and/or full spectrum radiation, comprising:
 - a) a base;
 - b) a rotatable means for holding a sample of said biological fluid;
 - c) a means for rotating said sample holding means; and
 - d) a means connected to said base for supporting said sample holding means.
10. An apparatus of claim 9, further including a reflector disposed between said sample holding means and said base.
11. A therapeutic method for treating infections, inflammatory and circulatory disorders comprising:
 - a) removal of a biological fluid from a patient;
 - b) irradiating said biological fluid sample with solar radiation; and
 - c) reinfusing said irradiated biological fluid into said patient.
12. A therapeutic method for treating infections, inflammatory and circulatory disorders comprising:
 - a) removal of a biological fluid from a patient;
 - b) irradiating said biological fluid sample with full spectrum radiation; and
 - c) reinfusing said irradiated biological fluid into said patient.
13. The therapeutic method of claim 11, wherein said patient is a human.

14. The therapeutic method of claim 11, wherein said fluid is selected from the group consisting of blood, plasma, serum, platelet-rich-plasma or some other fraction of blood.
15. The therapeutic method of claim 12, wherein said patient is a human.
16. The therapeutic method of claim 12, wherein said fluid is selected from the group consisting of blood, plasma, serum, platelet-rich-plasma or some other fraction of blood.

FIGURE



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/19292

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A01N 1/02; A61M 37/00; HO1J 3/14
US CL : 435/2; 604/4; 250/234

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/2; 604/4; 250/234

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Biosis, Medline, Napralert, Health and Wellness, APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| A,P | US 5,798,523 A (VILLENEUVE et al.) 25 August 1998. | 9,10 |
| A | WO 95/02325 A1 (BAXTER INTERNATIONAL INC.) 26 January 1995. | 9,10 |
| Y | SELVAAG, E. Photohemolysis due to oral antidiabetic drugs. Journal of Toxicology - Cutaneous and Ocular Toxicology. 1997, Vol. 16, No. 4, pages 217-226, especially abstract. | 1-8 |
| Y | Database Biosis, AN 80:179168, DURDEYEV et al. Dynamics of densimetric blood indexes under the effect of concentrated sunlight. Izv Akad Nauk Turkm Ssr Ser Biol Nauk 1978, No. 6, pages 81-83. | 1-8 |

 Further documents are listed in the continuation of Box C. See patent family annex.

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